

### ***Amendments to the Claims***

The listing of claims will replace all prior versions, and listings of claims in the application.

1. (currently amended) A method for isolation of biological macromolecules, said method comprising contacting ~~at least one filter~~ a filtration apparatus with a biological sample comprising ~~the said~~ biological macromolecules of interest, ~~wherein the pore size of said filter increases in the direction of sample flow; wherein genomic DNA comprised by said biological sample is sheared by said filter~~ said filtration apparatus comprising a first filter on top of a second filter such that said first filter is contacted with said biological macromolecules before said second filter, and said first filter having a pore size smaller than said second filter

2. (original) The method of claim 1, wherein said biological sample is a cellular lysate.

3. (original) The method of claim 2, wherein said cellular lysate is derived from eukaryotic cells.

4. (original) The method of claim 2, wherein said cellular lysate is derived from prokaryotic cells.

5. (original) The method of claim 3, wherein said eukaryotic cells are selected from the group consisting of fungi, fish cells, yeast cells, plant cells and animal cells.

6. (original) The method of claim 1, wherein said biological macromolecules are nucleic acid molecules.

7. (original) The method of claim 1, wherein said biological macromolecules are protein molecules.

8. (original) The method of claim 6, wherein said nucleic acid molecules are RNA molecules.

9. (original) The method of claim 8, wherein said RNA molecules are mRNA molecules.

10. (original) The method of claim 6, wherein said nucleic acid molecules are DNA molecules.

11. (original) The method of claim 10, wherein said DNA molecules are vectors or plasmids.

12. (cancelled)

13. (cancelled)

14. (cancelled)

15. (cancelled)

16. ( currently amended)      The method of claim ~~15~~ 1, wherein said pore size of said second filter ~~layer~~ is about 1  $\mu\text{m}$  to 500  $\mu\text{m}$ .

17. ( currently amended)      The method of claim 16, wherein said pore size of said second filter ~~layer~~ is about 10  $\mu\text{m}$  to 70  $\mu\text{m}$ .

18. ( currently amended)      The method of claim 17, wherein said pore size of said second filter ~~layer~~ is about 20  $\mu\text{m}$ .

19. (cancelled)

20. (cancelled)

21. ( currently amended)      The method of claim ~~13~~ 1, wherein said first filter ~~layer~~ comprises pores of sufficient size to retard the flow of cellular debris and particles.

22. ( currently amended)      The method of claim 21, wherein said pores of said first filter ~~layer~~ are about 0.1  $\mu\text{m}$  to 1.0  $\mu\text{m}$  in diameter.

23. ( currently amended)      The method of claim 21, wherein said pores of said first filter ~~layer~~ are about 0.2  $\mu\text{m}$  in diameter.

24. ( currently amended)      The method of claim ~~43~~ 1, wherein said second filter ~~layer~~ is comprised of ~~polyethylene, polypropylene or a combination thereof~~ glass fibers, silica, paper, cellulose, nitrocellulose, diatomaceous earth, and acetylated cellulose.

25. ( currently amended)      The method of claim ~~43~~ 1, wherein said first filter ~~layer~~ is comprised of one or more materials selected from the group consisting of hydrophobic polysulfone, hydrophilic polyether sulfone, cellulose, acetylated cellulose, nitrocellulose, polyester, polyolefin, scintered polyethylene, porous ceramics, silica, polypropylene, paper, and polysaccharide.

26. (cancelled)

27. ( currently amended)      The method of claim 26, wherein said first filter ~~layer is comprised of regenerated cellulose, with a~~ has an average pore size of about 0.2  $\mu\text{m}$ , and said second filter ~~layer is comprised of polyethylene or polypropylene, with~~ has an average pore size of about 20  $\mu\text{m}$ .

28. ( currently amended)      The method of claim 1, wherein said first filter is provided in a form selected from the group consisting of wafer, cylindrical, rectangular, beads, gels, square, cartridge, swab tip, plug, frit, membrane, sheets or inserts.

29. (currently amended) The method of claim 1, wherein said ~~filter~~ filtration apparatus is provided in a form that is suitable to be inserted into a tube, microspin tube, microfuge tube, spin cartridge, vial, ampule, bag or suitable to fit multi-well plates typically used in processing of multiple samples, including, 6-well plates, 12-well plates, 24-well plates, 48-well plates, 96-well plates, 384-well plates, or suitable to fit into other plate sizes such as 35 mm plates, 60 mm plates, 100 mm plates, or 150 mm plates.

30. (original) The method of claim 1, wherein the flow of the sample is facilitated by centrifugation, gravity, pressure, vacuum, or any combination thereof.

31. (currently amended) A method for isolation of biological macromolecules, said method comprising;

(a) contacting cells or cellular source containing the macromolecules of interest with a composition capable of lysing all or substantially all of said cells to give a lysate; and

(b) contacting the lysate with a ~~filter~~ filtration apparatus, wherein the ~~filter apparatus~~ filtration apparatus comprises two or more filters, and ~~wherein the pore size increases in the direction of sample flow; with a first filter on top of a second filter such that said first filter is contacted with said lysate before said second filter, and said first filter having a pore size smaller than said second filter; and~~

(c) promoting the flow ~~of the sample~~ through the ~~filter~~; filtration apparatus.

~~wherein genomic DNA comprised by said cells or cellular source is sheared by said filter.~~

32. -54. (cancelled)

55. (currently amended) A process for isolating biological macromolecules comprising, separating a lysed natural source in a sample by filtration, wherein said sample is passed through a filter, ~~the pore size of said filter increasing in the direction of sample flow through the filter~~ filtration apparatus comprising a first filter on top of a second filter such that said first filter is contacted with said biological macromolecules before said second filter, and said first filter having a pore size smaller than said second filter; ~~wherein genomic DNA comprised by said sample is sheared by said filter.~~

56. (currently amended) The process according to claim 55, wherein the ~~sample~~ flow through the filter filtration apparatus is promoted by applying positive or negative pressure, or by gravity, or by gravity increased by centrifugation, or by a combination thereof.

57. (original) The process according to claim 55, wherein said nucleic acid is plasmid DNA or genomic DNA having a size of from 1 to 50 kb (kilo base pairs).

58. (cancelled)

59. (cancelled)

60. (cancelled)

61. ( currently amended)      The process according to claim 55, wherein said ~~sample is passed through a two-layered filter bed wherein the first filter layer has a pore size of from 0.1 to 1.0  $\mu$ m, and the second filter layer has a pore size of from 1 to 500  $\mu$ m.~~

62. ( currently amended)      The process according to claim 55, wherein said ~~first filter layers of said filter comprises one or more filter layers are composed of sintered polyethylene, polypropylene, polytetrafluorethylene, glass, silica gel, alumina, or packed diatomaceous earth, e.g., cellite or silica gel, interwoven or cemented non-wovens of polypropylene, polyester, glass fibers and [[ ]] silica, as well as paper, compressed paper, paper non-wovens, hydrophobic polysulfone, hydrophilic polyether sulfone, cellulose, acetylated cellulose, nitrocellulose, polyester, polyolefin, scintered polyethylene, porous ceramics, silica, and polysaccharide. one or more materials selected from the group consisting of hydrophobic polysulfone, hydrophilic polyether sulfone, cellulose, acetylated cellulose, nitrocellulose, polyester, polyolefin, scintered polyethylene, porous ceramics, silica, polypropylene, paper, and polysaccharide.~~

63. ( currently amended)      The process according to claim 55, wherein wherein said second filter layer is comprised of polyethylene, polypropylene or a combination thereof glass fibers, silica, paper, cellulose, nitrocellulose, diatomaceous earth, and acetylated cellulose.

64-65. (cancelled)

66. (new) The method of any of claims 1, 31, or 55, wherein said second filter shears genomic DNA.